ultraviolet-absorbing sunglasses under bright outdoor conditions seems prudent. It also seems prudent to provide some extra ultraviolet filtration for people who have had their lens removed by cataract surgery. Manufacturers have responded to the latter concerns by marketing spectacles and intraocular lenses that block all light below 400 nm (the cutoff for a human lens). Unfortunately, the manufacturers of sunglasses have not been so explicit about the characteristics of their products. Ordinary glass and plastic absorb the far ultraviolet (below 350 nm) and some manufacturers advertise such lenses as "UV absorbing," which is misleading because light between 350 and 450 nm may still be transmitted and may be damaging.

To purchase sunglasses for ultraviolet protection, I suggest asking the vendor for information about spectral characteristics. An effective sunglass for retinal protection should block not only the full range of ultraviolet, but also the deep blue end of the spectrum. Because of the reduction in blue light transmission, such glasses often have a yellowish or amber tint in addition to whatever degree of darkness they may have.

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Recessive Human Cancer Genes

RECENT OBSERVATIONS in retinoblastoma, a relatively rare malignant intraocular tumor in childhood, have provided evidence for a new class of human cancer genes. It is generally accepted that division and differentiation of cells in higher organisms are regulated by many controls and that tumors arise through the accumulation of several changes releasing the cells from constraints on growth. Statistical data suggest that two successive mutationlike changes are required for the development of retinoblastoma, three to four for leukemias and six to seven for carcinomas.

The first evidence for the presence of recessive cancer genes in humans was provided by retinoblastoma. It has been known for more than 15 years that in 2% to 3% of retinoblastoma cases, a loss or deletion of region q14 of chromosome 13 was associated with the appearance of retinoblastoma. Observations that the loss or deletion of both 13 chromosomes had occurred in the tumor of one patient suggested that the two "mutations" postulated by Knudson as being necessary for retinoblastoma to develop might be the loss or inactivation of both copies of a recessive gene on chromosome 13 perhaps necessary for differentiation. This concept has been strengthened by the subsequent observation that in nearly 80% of all retinoblastomas examined, both sporadic and familial, chromosome 13 becomes homozygous, presumably for the mutant or abnormal regulator gene at the retinoblastoma locus. Recently osteosarcoma, a tumor known to occur frequently in families with retinoblastoma, has been shown to be homozygous for the same 13 chromosome, suggesting that this "regulator gene" may normally limit bone as well as retinal growth.

The recessive "regulatory" gene model in humans has subsequently been shown to hold for Wilms' tumor where loss of both copies of a recessive cancer gene on the short arm of chromosome 11 has been found. This same locus seems to be involved as well in some other childhood tumors, specifically rhabdomyosarcoma and hepatoblastoma.

It is not surprising that the childhood tumors arise from relatively fewer events than adult tumors because they appear earlier in life. It is clear from the experience with retinoblastoma that specific DNA changes, whether inherited or not, are inherently a part of the tumorigenic process.

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Diabetic Macular Edema

MACULAR EDEMA (swelling of the central, reading part of the retina) is the leading cause of vision loss in the diabetic population. Although this vision loss is usually not as severe as that caused by bleeding inside the eye, patients with this complication can lose reading and driving vision. Depending on a patient's age at diagnosis of diabetes, one population-based study found the prevalence rate of macular edema to vary from 0% to 3% in those patients with diabetes for less than 5 years and 28% to 29% for those patients with diabetes for 20 or more years. A recently published national collaborative study has shown that photocoagulation is an effective treatment for many of these patients.

The beneficial effect of photocoagulation treatment was shown in those eyes with early diabetic retinopathy (scattered retinal hemorrhages, microaneurysms and exudates) and clinically significant macular edema. Clinically significant macular edema is defined as:

- thickening of the retina at or within 500 microns of the center of the macula (located one disc diameter temporal to the optic nerve),
- hard exudates at or within 500 microns of the center of the macula if associated with thickening of adjacent retina and
- a zone or zones of retinal thickening one disc area or larger in size, any part of which is within one disc diameter of the center of the macula.

Thus, diabetic patients with early diabetic retinopathy and one or more of the above findings should be considered for focal or limited-scatter photocoagulation treatment of the macula. Whether to treat macular edema in eyes with more advanced retinopathy (venous dilatation and beading, intraretinal microvascular abnormalities, cotton wool spots or retinal or disc neovascularization) was left to the discretion of the treating ophthalmologist. The study showed a beneficial trend of treatment in these eyes, but the results were not conclusive. Panretinal photocoagulation treatment should be applied if a high-risk characteristic is present as defined in a prior national collaborative study.

About 4,000 patients will continue to be followed as part of the Early Treatment Diabetic Retinopathy Study to answer the study's two remaining questions:

1. When in the course of diabetic retinopathy is it most effective to initiate photocoagulation therapy?

2. Is aspirin effective in altering the course of diabetic retinopathy?

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Treatment of Macular Pucker

THE TERM MACULAR PUCKER refers to membranes overlying or distorting the macula or foveal region of the retina, causing a significant reduction in central vision. These membranes may occur spontaneously; they are also a major cause of poor central vision following surgical correction of a retinal detachment due to a retinal hole. Epiretinal membranes are often seen in diabetic retinal disease.

Puckering of the macula occurs when contraction of the preretinal membranes causes wrinkling of the underlying retina. This is accompanied by distortion and reduction in visual acuity. These preretinal membranes may very rarely separate from the retina spontaneously, with improvement in vision.

Vitreous surgical techniques can be used to remove epiretinal membranes. The success rate of this operation is high, with visual improvement occurring in up to 90% of cases. The greatest amount of improvement occurs in cases with the greatest degree of visual reduction. Vision limited to counting fingers may be improved to the 20/100 level even after several years of reduced vision. Visual distortion may also improve significantly following surgical repair.

Complications are uncommon but do occur. They include retinal detachment, recurrence of the epiretinal membranes on rare occasions and cataract.

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Botulinum Toxin Therapy in the Management of Strabismus and Lid Disorders

IN 1973 Scott, Rosenbaum and Collins reported on the use of various drugs injected directly into the extraocular muscles of monkeys. The drugs used were diiosopropyl fluorophosphate, cobra neurotoxin, botulinum neurotoxin and alcohol. The goal was to discover a pharmacologic means of producing a long-term paralysis of the injected muscle while causing minimal systemic involvement. Botulinum toxin appeared to satisfy these requirements.

In 1981 Scott reported on the results of 132 injections in 42 humans. In 1982 he initiated a prospective multicenter clinical trial to evaluate the safety and efficacy of botulinum toxin under a Food and Drug Administration protocol. To date, more than 5,000 patients have been injected, and the study is still under way.

Six antigenically different types of botulinum toxin have been identified. Type A neurotoxin is the only one used pharmacologically at this time; it is a single polypeptide chain with a molecular weight of about 150,000.

Botulinum toxin appears to act by interfering with acetylcholine release from the nerve terminal. It acts on individual muscle terminals presynaptically, but apparently does not affect the electrical excitability or conduction in either the muscle or nerve. The doses used seem to be below the threshold of recognition by the immune system, thus allowing repeated injections.

The therapeutic principle of botulinum toxin in strabismus is to paralyze the injected muscle. The paralysis usually lasts four to eight weeks, during which time the antagonist muscle has a chance to contract or gain strength. When the pharmacologic effect wears off, the forces should then be balanced. In other words, the injected muscle will have undergone a weakening procedure or chemical "recession" and the antagonist muscle will have undergone contracture or a "resection." Botulinum toxin can also be used to prevent contracture of a muscle when the antagonist muscle is paralyzed and when one is awaiting recovery of that paralysis, such as in a case of acute sixth nerve palsy.

Adults are injected using only topical anesthesia. A special portable electromyographic recorder is attached to a monopolar or bipolar electrode in a uniquely designed hypodermic needle. In the tip of the hypodermic needle is the electrode used for proper placement of the neurotoxin in the muscle. The needle is inserted subconjunctivally and is then passed into the desired muscle, with that muscle undergoing contracture. Usually 0.1 ml of toxin is injected. The dosages range between 1×10^{-3} and 1×10^{-2} μg, or 1/200th the median lethal dose level for humans.

Considerable clinical experience has occurred during the past several years. The absolute indications are not yet completely clear, however, although several principles seem to be emerging. There is much more widespread usage of the drug in adults than in children because of the need to use ketamine hydrochloride anesthesia for children and the need for reinjection, at least at current protocol dose schedules. There is more enthusiasm for injecting the horizontal rectus muscles than the vertical rectus muscles, as they are easier to inject. Also, in superior rectus injections there is involvement of the lid, and in the inferior rectus injections, the inferior oblique muscle is involved. The mean correction per injection is about 20 prism diopters. Thus, the ideal patient appears to be one with horizontal strabismus of small to moderate size.

There are several strabismic conditions for which botulinum toxin injection is ideal. These include chronic sixth nerve palsy when accompanied by a transposition procedure, acute sixth nerve palsy to prevent secondary contracture and acute thyroid ophthalmopathy when surgical treatment is not yet indicated. Phthisis, active inflammation or severe glau-